

LAY ABSTRACT

Vitamin B12 (cobalamin) deficiency is very common in the US and world-wide. The risk of deficiency increases with aging, with an estimated 25% of persons over age 65 deficient or depleted in the US. Based on a serum cobalamin level below 150 pmol/L as the indicator of B12 deficiency, and 150-221 pmol/L as the indicator of marginal status, we confirmed that observed B12 deficiency is also common in Californian elderly; in a representative sample of 1545 Latinos aged 60 year and above in the Sacramento region, 6.5% had deficiency and an additional 16% had marginal status.

At least 40% of the elderly with low serum cobalamin have this problem because they cannot absorb the vitamin from food. Loss of gastric function (gastric atrophy) and low acid secretion by the stomach are thought to be involved. Underlying causes probably include chronic infection with the bacterium *Helicobacter pylori* which causes the stomach to produce less acid and atrophy over time, and/or an overgrowth of other bacteria in the stomach and upper intestine which compete for the vitamin B12.

Most elderly can absorb synthetic, crystalline forms of the vitamin, such as those added to fortified cereals or used in supplements, but we do not know whether elderly absorb these forms of vitamin B12 as well as younger people do. Thus, although it is generally recommended that older people obtain a higher proportion of their B12 from fortified cereals and supplements, it is not clear how much they need to consume from these sources. This question is particularly relevant today because although flour has to be fortified with folic acid in the United States, it is not yet fortified with vitamin B12 – precisely because it is unclear how much to add and whether elderly with gastric atrophy will be able to absorb enough. An additional concern is that folic acid fortification may worsen the neurological and cognitive deterioration that can occur with vitamin B12 deficiency, as suggested in some recent studies – suggesting that flour fortification with vitamin B12 in addition to folic acid may be especially important. One purpose of the proposed research is therefore to determine whether elderly with gastric atrophy absorb vitamin B12 from fortified bread as well as do elderly without gastric atrophy.

Another issue concerning the ability of older persons to absorb vitamin B12 is that their ability to absorb the vitamin from food is rarely tested. When older people are found to have a low serum cobalamin level, medical practitioners often ignore this problem until the level becomes even lower, or symptoms of deficiency (such as nerve damage) appear. Alternatively they prescribe B12 injections every few months, or high daily doses by mouth, for the rest of the person's life. However, it is possible, but has not yet been tested, that treating the *Helicobacter pylori* and bacterial overgrowth, which can be done with the same medicines, will enable the stomach to recover so the person can regain their ability to absorb vitamin B12 from food.

Our approach to these questions uses a novel method to assess cobalamin absorption. Cobalamin labeled with very low doses of radioactivity will be added to bread as a fortificant, at a level similar to that which might be added in flour fortification. Persons 60 years and older will have their serum cobalamin levels checked to identify those with low levels, who will then be checked for gastric atrophy using serum markers, direct visualization of the stomach and biopsy, where appropriate. Ten people with markers of gastric atrophy, and ten without, will consume the labeled bread, and their absorption of the vitamin compared by following the amount of radioactivity in the blood and urine during the next 24 hours. Those with gastric atrophy symptoms will have their stomach examined, and take medication to eliminate *H. pylori* and bacterial overgrowth. One month later they will repeat the test of cobalamin absorption from labeled bread, to see if the treatment has improved absorption. The results will show whether vitamin B12 fortification of bread could be useful to improve vitamin B12 status of people with gastric atrophy, and whether their B12 absorption can be improved by treatment with antibiotics to eradicate *Helicobacter pylori* and other microorganisms.